

Applicants: Philip O. Livingston and Friedhelm Helling
Serial No.: 08/196,154
Filed: November 16, 1995
Page 2

Please amend the subject application as follows:

Amendment to the Claims:

This listing of claims will replace all prior versions,
and listings, of claims in the application:

Listing of the Claims:

1.-118. (Cancelled)

~~119.~~ (Currently Amended) A composition which comprises:

- a) a conjugate of (i) a derivative of a GM2 ganglioside which GM2 ganglioside comprises an unaltered sphingosine base, wherein the derivative differs from the GM2 ganglioside solely by having an altered sphingosine base which retains only C1 through C4 from the unaltered sphingosine base of the GM2 ganglioside, and (ii) Keyhole Limpet Hemocyanin, wherein the GM2 ganglioside derivative is covalently bound to Keyhole Limpet Hemocyanin by a stable amine bond between the C-4 carbon of the altered sphingosine base and a nitrogen of an ϵ -aminolysyl group of Keyhole Limpet Hemocyanin;
- b) QS-21; and
- c) a pharmaceutically acceptable carrier,

wherein the amount of the conjugated GM2

ganglioside derivative is an amount between about 1 µg and about 200 µg, the amount of QS-21 is an amount between about 10 µg and about 200 µg, the GM2 derivative:Keyhole Limpet Hemocyanin molar ratio is from 200:1 to 1400:1, and the relative amounts of such conjugate and QS-21 is effective to stimulate or enhance production in a subject of an antibody to the GM2 ganglioside.

120.-125. (Cancelled)

2 ✓ 126. (Previously Presented) The composition of claim 119 wherein the amount of QS-21 is about 50 µg.

3 ✓ 127. (Previously Presented) The composition of claim 119 wherein the amount of QS-21 is about 200 µg.

128. (Cancelled)

4 ✓ 129. (Currently Amended) The composition of claim 119 which comprises:

- a) a conjugate of (i) a derivative of a GM2 ganglioside which GM2 ganglioside comprises an unaltered sphingosine base, wherein the derivative differs from the GM2 ganglioside solely by having an altered sphingosine base which retains only C1 through C4 from the unaltered sphingosine base of the GM2 ganglioside, and (ii) Keyhole Limpet Hemocyanin, wherein the GM2 ganglioside derivative is covalently bound to Keyhole

Limpet Hemocyanin by a stable amine bond between the C-4 carbon of the altered sphingosine base and a nitrogen of an ϵ -aminolysyl group of Keyhole Limpet Hemocyanin;

b) QS-21; and

c) a pharmaceutically acceptable carrier,

wherein the amount of the conjugated GM2 ganglioside derivative is present in an amount between about 1 μ g and about 200 μ g, the amount of QS-21 is about 100 μ g, the GM2 derivative:Keyhole Limpet Hemocyanin molar ratio is from 200:1 to 1400:1, and the relative amounts of such conjugate and QS-21 is effective to stimulate or enhance production in a subject of an antibody to the GM2 ganglioside.

130. (Previously Presented) A method of treating a subject afflicted with melanoma which comprises administering to said subject an amount of the composition of claim 129 effective to stimulate or enhance production in a subject of an antibody to the GM2 ganglioside and to thereby treat said melanoma in said subject.

131. (Currently Amended) A method of stimulating or enhancing production of an antibody directed to the GM2 ganglioside in a subject which comprises administering to the subject an effective amount of a composition which comprises:

- a) a conjugate of (i) a derivative of a GM2 ganglioside which GM2 ganglioside comprises an unaltered sphingosine base, wherein the derivative differs from the GM2 ganglioside solely by having an altered sphingosine base which retains only C1 through C4 from the unaltered sphingosine base of the GM2 ganglioside, and (ii) Keyhole Limpet Hemocyanin, wherein the GM2 ganglioside derivative is covalently bound to Keyhole Limpet Hemocyanin by a stable amine bond between the C-4 carbon of the altered sphingosine base and a nitrogen of an ϵ -aminolysyl group of Keyhole Limpet Hemocyanin;
- b) QS-21; and
- c) a pharmaceutically acceptable carrier,

wherein the amount of the conjugated GM2 ganglioside derivative is an amount between about 1 μ g and about 200 μ g, the amount of QS-21 is an amount between about 10 μ g and about 200 μ g, the GM2 derivative:Keyhole Limpet Hemocyanin molar ratio is from 200:1 to 1400:1, and the relative amounts of such conjugate and QS-21 is effective to stimulate or enhance production in a subject of an antibody directed to the GM2 ganglioside.

X 132. (Currently Amended) A method of treating a human subject having cancer which comprises administering to the subject an effective amount of a composition which comprises:

- a) a conjugate of (i) a derivative of a GM2 ganglioside which GM2 ganglioside comprises an unaltered sphingosine base, wherein the derivative differs from the GM2 ganglioside solely by having an altered sphingosine base which retains only C1 through C4 from the unaltered sphingosine base of the GM2 ganglioside, and (ii) Keyhole Limpet Hemocyanin, wherein the GM2 ganglioside derivative is covalently bound to Keyhole Limpet Hemocyanin by a stable amine bond between the C-4 carbon of the altered sphingosine base and a nitrogen of an ϵ -aminolysyl group of Keyhole Limpet Hemocyanin; and
- b) QS-21; and
- c) a pharmaceutically acceptable carrier,

wherein the amount of the conjugated GM2 ganglioside derivative is an amount between about 1 μ g and about 200 μ g, the amount of QS-21 is an amount between about 10 μ g and about 200 μ g, the GM2 derivative:Keyhole Limpet Hemocyanin molar ratio is from 200:1 to 1400:1, and the relative amounts of such conjugate and QS-21 is effective to stimulate or enhance production in a subject of an antibody to the GM2 ganglioside and thereby treat the subject.

133. (Previously Presented) The method of claim 132, wherein the cancer is of epithelial origin.

- 9 134. (Previously Presented) The method of claim ~~132~~⁷,
wherein the cancer is of neuroectodermal origin.
- 10 135. (Previously Presented) The method of claim ~~134~~⁹,
wherein the cancer of neuroectodermal origin is
a melanoma.
- 11 136. (Previously Presented) The method of claim ~~131~~⁶ or
132, wherein the administering is effected at
two or more sites.
- 12 137. (Previously Presented) The method of claim ~~136~~¹¹,
wherein the administering is effected at three
sites.
- 13 138. (Previously Presented) The method of claim ~~131~~⁶ or
132, wherein the composition is administered
subcutaneously to said subject.
- 14 139. (Previously Presented) The method of claim ~~138~~¹³,
wherein the composition is administered to said
subject at two-week intervals.
- 15 140. (Previously Presented) The method of claim ~~138~~¹³,
wherein the composition is initially
administered to said subject at weekly
intervals.
- 16 141. (Previously Presented) The method of claim ~~131~~⁶ or
132, wherein the composition to be administered
is prepared prior to administration to the

Applicants: Philip O. Livingston and Friedhelm Helling
Serial No.: 08/196,154
Filed: November 16, 1995
Page 8

subject by mixing the conjugate and QS-21.

17/ 142. (Previously Presented) The method of claim 141,
wherein the conjugate and QS-21 are mixed on the
day of administration to the subject.

143. (Cancelled)